

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claims 1-13 (Canceled).

14. (Withdrawn) A method for rapid angiogenensis targeting comprising administering an antibody conjugate of claim 20.

15. (Withdrawn) The method according to claim 14 for immunoscintigraphic detection of angiogenesis.

16. (Withdrawn) The method according to claim 15 for detecting diseases characterized by vascular proliferation.

17. (Withdrawn) The method according to claim 14, wherein the antibody localizes the target tissue three to four hours after its injection.

Claim 18 (Canceled).

19. (Withdrawn) A method for therapy of a tumour or a disease characterized by vascular proliferation comprising administering an antibody conjugate of claim 20.

20. (Currently Amended) The conjugate comprising an antibody with an affinity (Kd) for the ED-B domain of fibronectin of less than about 54pM, and a molecule which induces blood coagulation and blood vessel occlusion.

21. (Previously Presented) The conjugate according to claim 20 wherein the molecule which induces blood coagulation and blood vessel occlusion is a photoactive molecule.

22. (Previously Presented) The conjugate according to claim 21 wherein the photoactive molecule is a photosensitizer.

23. (Previously Presented) The conjugate according to claim 22 wherein the photosensitizer absorbs at a wavelength above 600 nm.

24. (Previously Presented) The conjugate according to claim 22 wherein the photosensitizer is a derivative of tin (IV) chlorine e6.

25. (Withdrawn) The method for the treatment of an angiogenesis-related a pathology comprising injecting a conjugate according to claim 20.

26. (Withdrawn) The method for the treatment of an angiogenesis-related a pathology comprising injecting a conjugate according to claim 22, followed by irradiation.

27. (Withdrawn) The method according to claim 26 wherein the angiogenesis-related pathology treated is caused by a or associated with ocular angiogenesis.

28. (Previously Presented) The conjugate according to claim 20, wherein said affinity is 27 to 54pM.

29. (Previously Presented) The conjugate according to claim 28 wherein the molecule which induces blood coagulation and blood vessel occlusion is a photoactive molecule.

30. (Previously Presented) The conjugate according to claim 29 wherein the photoactive molecule is a photosensitizer.

31. (Previously Presented) The conjugate according to claim 30 wherein the photosensitizer absorbs at a wavelength above 600 nm.

32. (Previously Presented) The conjugate according to claim 30 wherein the photosensitizer is a derivative of tin (IV) chlorine e6.

33. (Previously Presented) The conjugate according to claim 20, wherein the antibody is an scFv antibody.

34. (Previously Presented) The conjugate according to claim 33, wherein the antibody is a recombinant antibody.

Claim 35 (Canceled)

36. (Withdrawn – Currently Amended) The conjugate of claim 38 further comprising comprising an antibody with an affinity (Kd) for the ED-B domain of fibronectin of less than 54pM, and a molecule which induces blood coagulation and blood vessel occlusion wherein said antibody comprises the following amino acid sequence

VH domain (SEQ ID NO: 19)

|                            |                            |                            |
|----------------------------|----------------------------|----------------------------|
| <u>E V Q L L E S G G G</u> | <u>L V Q P G G S L R L</u> | <u>S C A A S G F T F S</u> |
| <u>S F S M S W V R Q A</u> | <u>P G K G L E W V S S</u> | <u>I S G S S G T T Y Y</u> |
| <u>A D S V K G R F T I</u> | <u>S R D N S K N T L Y</u> | <u>L Q M N S L R A E D</u> |
| <u>T A V Y Y C A K P F</u> | <u>P Y F D Y W G Q G T</u> | <u>L V T V S S</u>         |

Linker (SEQ ID NO: 20)

G D G S S G G S G G A S T G

VL domain (SEQ ID NO: 21)

E I V L T Q S P G T      L S L S P G E R A T      L S C R A S Q S V S

|                            |                            |                            |
|----------------------------|----------------------------|----------------------------|
| <u>S S Y L A W Y Q Q K</u> | <u>P G Q A P R L L I Y</u> | <u>Y A S S R A T G I P</u> |
| <u>D R F S G S G S G T</u> | <u>D F T L T I S R L E</u> | <u>P E D F A V Y Y C Q</u> |
| <u>Q T G R I P P T F G</u> | <u>Q G T K V E I K</u>     |                            |

at least one mutation in one or more residues of its CDR regions, wherein the affinity of the antibody for the ED-B domain is increased, and ~~wherein said mutation(s) are in at least one residue corresponding to residues 31-33, 50, 52 and/or 54 of the VH domain of SEQ ID NO: 30 and/or residues 32 and/or 50 of the VL domain of SEQ ID NO: 32.~~

37. (Currently Amended) The conjugate according to claim 28, wherein the antibody binds to the ED-B domain of fibronectin with a  $K_d$  of about 54 pM.

38. (Previously Presented) The conjugate according to claim 28 with the following amino acid sequence

VH domain (SEQ ID NO: 19)

|                     |                     |                     |
|---------------------|---------------------|---------------------|
| E V Q L L E S G G G | L V Q P G G S L R L | S C A A S G F T F S |
| S F S M S W V R Q A | P G K G L E W V S S | I S G S S G T T Y Y |
| A D S V K G R F T I | S R D N S K N T L Y | L Q M N S L R A E D |
| T A V Y Y C A K P F | P Y F D Y W G Q G T | L V T V S S         |

Linker (SEQ ID NO: 20)

G D G S S G G S G G A S T G

VL domain (SEQ ID NO: 21)

|                     |                     |                     |
|---------------------|---------------------|---------------------|
| E I V L T Q S P G T | L S L S P G E R A T | L S C R A S Q S V S |
| S S Y L A W Y Q Q K | P G Q A P R L L I Y | Y A S S R A T G I P |
| D R F S G S G S G T | D F T L T I S R L E | P E D F A V Y Y C Q |

Q T G R I P P T F G

Q G T K V E I K

39. (Currently Amended) The conjugate according to claim 20, wherein said affinity is ~~about~~ 50-54pM.

40. (Previously Presented) The conjugate according to claim 20, wherein the fibronectin is human.

41. (Previously Presented) The conjugate according to claim 20, wherein the antibody comprises the VH domain of SEQ ID 19.

42. (Previously Presented) The conjugate according to claim 20, wherein the antibody comprises the VL domain of SEQ ID 21.

43. (Currently Amended) The conjugate according to claim 35 36, wherein the number of mutations is 1-3.

Claims 44-48 (Canceled)

49. (Withdrawn) The method of claim 16 wherein said disease is diabetic retinopathy, age-related macular degeneration or a tumour.

50. (Withdrawn) The method of claim 17 wherein said antibody localizes in three hours.

51. (New) The conjugate of claim 35 comprising an antibody with an affinity (Kd) for the ED-B domain of fibronectin of less than 54pM, and a molecule which induces blood coagulation and blood vessel occlusion wherein said antibody comprises the following amino acid sequence  
VH domain (SEQ ID NO: 19)

|            |            |            |
|------------|------------|------------|
| EVQLLESGGG | LVQPGGSLRL | SCAASGFTFS |
| SFSMSWVRQA | PGKGLEWVSS | ISGSSGTTYY |
| ADSVKGRFTI | SRDNSKNTLY | LQMNSLRAED |
| TAVYYCAKPF | PYFDYWGQGT | LTVSS      |

Linker (SEQ ID NO: 20)

**G D G S S G G S G G A S T G**

VL domain (SEQ ID NO: 21)

|            |            |            |
|------------|------------|------------|
| EIVLTQSPGT | LSLSPGERAT | LSCRASQSVS |
| SSYLAWYQQK | PGQAPRLLIY | YASSRATGIP |
| DRFSGSGSGT | DFTLTISRLE | PEDFAVYYCQ |
| QTGRIPPTFG | QGTKVEIK   |            |

in which said residues 31-33, 50, 52 and/or 54 of the VH domain of SEQ ID NO: 30 and/or residues 32 and/or 50 of the VL domain of SEQ ID NO: 32 are substituted by a different natural amino acid.